

*Integrating the Marginalized: A Neuropsychosocial Perspective of Autism Spectrum
Disorders in American Society*

An Honors Thesis (PSYS 497)

by

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April 2013

Expected Date of Graduation

May 2013

Abstract

Autism spectrum disorders (ASDs) are neurodevelopmental disorders characterized by social and communicative deficits, and repetitive behaviors, and generally onset before three years of age.

ASDs have come more and more into the public consciousness since the 1980s because diagnosis rates have sharply risen (2012 CDC estimates place prevalence at 1 child per 88).

Despite the dramatic increase in societal awareness of ASDs, societal understanding of their biology and psychology has lagged. Examining ASDs through biological, neuropsychological, and sociocultural perspectives will facilitate a more complete understanding of what ASDs are, where they come from, and how society can better integrate affected individuals in the future.

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Acknowledgements

I would like to express my gratitude for the wisdom and guidance of my thesis advisor, Dr. Stephanie Simon-Dack. Her suggestions and counsel were invaluable for my navigation of the thesis process. Without her time and knowledge, this thesis would not have been possible.

I would also like to thank the members of my PSYS 499 honors thesis course, especially the course's supervisor, Dr. Thomas Holtgraves. His constructive criticism regarding my content and organization greatly improved the total quality of my thesis, and his clarification questions helped me refocus on its purpose. Thanks also to the other students in my PSYS 499 course: Haley Armstrong, Kaitlin Pickett, and Carin Smith, whose ideas and encouragement let me improve my work in a friendly environment.

I would be remiss if I did not also thank my family and friends for their endless support as I undertook this project.

Author's Statement

The idea for this thesis originated when I was brainstorming psychological concepts and disorders that I did not know much about but wanted to study. Of all the disorders on the list, autism was the one that I felt I should know much more about than I did. The societal component of the project came about when I asked my friends and family what *they* knew about autism. Most could not get past “Well, it’s a disorder...” and some couldn’t decide if it was a disease but focused more on the fact that a lot of kids are getting it. It was at this point that I realized the benefit of writing a thesis about ASDs: it would not only enrich my own understanding but hopefully the understanding of others who read it as well, whether they are academics or laypeople. Hopefully, this understanding can turn into empathy and caring, and eventually into the integration of individuals with ASDs into society. Autism is an amazing disorder in both its complexity and its expression, and hopefully bringing it into the light will help achieve this goal.

Integrating the Marginalized: A Neuropsychosocial Perspective of Autism Spectrum Disorders in American Society

A marked increase in autism spectrum disorder (ASD) diagnoses in the United States since the 1980s necessitates an enhanced understanding of the physiological, psychological, and sociocultural underpinnings of the disorder, which will permit improved cultural acceptance and understanding of affected individuals. ASDs are neurodevelopmental disorders characterized by repetitive behaviors and impaired social interaction and communication, which typically have onset before three years of age. The variable presentation of autism is not well understood. Due to the wide array of alleged causes and the volume of diagnosed children, it is important to address autism through three channels: biological, neuropsychological, and sociocultural. The biological aspect is relevant because it explains genetic and neurological changes present in autism. The neuropsychological aspect offers prominent theories relating to how biology interacts with psychology to produce ASD symptomology. The sociocultural aspect is important because it discusses the current interaction of society and individuals with autism. Thus, the biological aspect leads into the neuropsychological, which leads into the sociocultural aspect. An integrative method of understanding autism comprised of these three channels will allow American society to better comprehend the complex biological and psychological mechanisms of autism, and create a more receptive and empathic incorporation of autistic individuals into society.

Definitions and Diagnosis

The autism spectrum is a diagnostic continuum of three major developmental disorders: Autism Disorder (AD), Asperger's Disorder, and Pervasive Developmental Disorder – Not Otherwise Specified (PDD-NOS) (Newschaffer et al., 2006). The autism spectrum's existence

speaks to the heterogeneous nature of autism, merging three disorders and countless phenotypes together as a continuum of clinically related symptomologies.

The word *autism* is commonly used in society and in research to encapsulate all ASDs, and will be used as such in this manuscript, but it does not mean AD per se. The term *neurotypical* will be used to describe individuals not on the autism spectrum.

Autism Disorder

The Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR) offers diagnostic criteria for AD based on three aspects of behavior: social interaction, communication, and repetitive behavior. Each aspect is comprised of four criteria, of which two from social interaction and one each from communication and repetitive behavior must be fulfilled (and the total fulfilled criterion count must be at least six) for positive diagnosis (See Table 1).

Children with AD often have difficulty developing spoken language, and speak rarely or atypically. One possible clinical feature of communicative abnormality in AD is echolalia, an involuntary vocal repetition of a sound in the environment, either ambient or another person's words. For instance, an echolalic individual may be asked, "do you want to go to the park?" and he may respond, "do you want to go to the park?... do you want to go to the park?... yes, I want to go to the park." Children with AD may also demonstrate pronoun reversal, a linguistic abnormality related to echolalia. In pronoun reversal, a child replaces pronouns in a sentence to refer to themselves or others with incorrect pronouns. For example, if a mother asks, "do you want to go to the park?," her child may say, "You want to go to the park," meaning that he would like to go. This seems to be linked to the difficulties individuals with ASD have with social understanding as well, because children with AD and pronoun reversal refer to themselves in

responses the same way that they are referred to in a prompt (Tager-Flusberg, Lord & Paul, 1997). In this case, the mother's use of *you* to refer to the child is coupled with the child's social-communicative deficit in understanding the differences between self and others (see mind-blindness theory below), resulting in the child using *you* for self-reference. Alternatively, pronoun reversal could be perceived as the child simply repeating what they were asked in an echolalic manner with incorrect pronouns. Pronoun reversal can be confusing for others who interact with ASD children, and if pronoun reversal occurs in tandem with echolalia, communication can become convoluted.

Individuals with AD tend to have difficulty forming social bonds with people other than their caregivers (Sigman, Dijamco, Gratier, & Rozga, 2004). Bauminger and Kasari (2000) found that among high-functioning individuals with AD, the quality of friendships, not the quantity, predicted feelings of satisfaction or loneliness. The underlying desire for social function flies in the face of commonly held beliefs that individuals with AD always prefer to be alone and do not feel lonely. There is thus a distinction between solitude (aloneness) and loneliness, and this distinction is often made in AD. From this distinction, it can be inferred that individuals with AD can and do feel lonely, and that solitude is not their only desired state.

Per the Repetitive Behavior Scale-Revised (Lam & Aman, 2007), repetitive behavior presentation in AD includes stereotypy, self-injurious behavior, compulsive behavior, need for sameness, ritualistic behavior, and restricted interest (see Table 2 for definitions and examples).

In addition to the core social, communicative, and behavioral symptoms, sensory processing disorders are very common in ASDs (Watling, Deitz, & White, 2001, as cited in Tomchek & Dunn, 2007). Greenspan and Weider (1997) reported that 100% of the 200 autistic participants in a retrospective chart review of developmental patterns demonstrated difficulties

with auditory responding (as cited in Tomchek & Dunn, 2007). Visual and tactile processing dysfunctions are also common, and when these domains are combined, attentional tasks may be affected (for more information about sensory processing issues, see “Neuropsychological Theories of ASDs” below).

Asperger’s Disorder

Asperger’s Disorder is diagnosed with several criteria, including a lack of social reciprocity, nonverbal action for social regulation, and enjoyment sharing, as well as preoccupation with components rather than wholes, repetitive behaviors, and impairment in sociocultural functioning. However, a hallmark of Asperger’s Disorder is a lack of clinically significant impairment in language or cognitive function, manifesting popularly as “high-functioning” autism (See Table 3). Individuals with Asperger’s Disorder differ from those with AD in that they do not experience major language impairments during development, and often display normal cognitive skills, which places the disorder closer to typicality on a functional continuum than AD or PDD-NOS. Asperger’s Disorder is included in the autism spectrum because its manifestation involves many pronounced autistic symptoms, but it does not match AD exactly. Daily struggles for children with Asperger’s Disorder may be centered more upon social deficits and insistence on sameness than upon communicating needs as in AD.

PDD-NOS

Diagnosis for PDD-NOS can be highly variable, because the only criterion is “severe and pervasive” impairment that does not meet diagnostic criteria for Pervasive Developmental Disorder, Schizophrenia, Schizotypal Personality Disorder, or Avoidant Personality Disorder. PDD-NOS is characterized by subclinical impairment or late onset in all three categories of AD (See Table 4). Individuals with PDD-NOS may experience severe overall sociocommunicative

impairments but not meet criteria for AD or Asperger's Disorder, or the onset of their symptoms may occur after 36 months. Hypothetically, a ten-year-old child with PDD-NOS could closely resemble a ten-year-old with AD in his social, communicative, and behavioral profile, but the difference in diagnosis was that the child with PDD-NOS did not show clinical deficits until 38 months as opposed to 35. PDD-NOS is included on the spectrum because it can be used to describe atypical autism cases, and positive diagnosis represents a segment of society that would not be included in diagnosis previously.

Changes in Diagnosis

The DSM-5, which will supersede the DSM-IV-TR, is scheduled for publication in May 2013. The main proposed change regarding ASDs is to combine AD, Asperger's Disorder, PDD-NOS, and childhood disintegrative disorder (a disorder in which development occurs normally for years, but then drastically shifts to autistic) into the single diagnostic category of ASD. This change would truly put the diagnoses on a spectrum, and because there would be only one ASD category instead of many, the clinical emphasis would be on assessing the severity of dysfunction and specific deficits rather than focusing on criteria checklists (American Psychiatric Association, 2013). Clinicians then may not be focused on categorizing a child as having AD, Asperger's Disorder, or PDD-NOS, but instead focus on a child's relative deficits within the ASD category. However, this change is not without resistance; Tony Attwood, an English psychologist and author of several books about Asperger's Disorder, believes that Asperger's Disorder is a very useful diagnostic tool because it is viewed more positively than AD or general "autism". Attwood stated: "the general public has either a neutral or fairly positive view of the term Asperger's syndrome, but if people are told they should be evaluated

for autism, they will say: ‘No, no, no. I can talk. I have a friend. What a ridiculous suggestion!’ So we will miss the opportunity to assess people” (Wallis, 2009).

Epidemiology

A major catalyst in public concern about ASDs is the drastic increase in ASD diagnoses over several decades. Fombonne (2005) offers an average male-to-female ASD ratio of 4.3:1. The Centers for Disease Control and Prevention (CDC, 2012) estimated ASD population prevalence at 1:88, with sex-specific prevalence at 1:54 for males and 1:252 for females. In a global study of ASD epidemiology studies, Elsabbagh et al. (2012) found the median prevalence estimate to be 62 cases per 10,000 people, and also found that data did not support socioeconomic, ethnic, or cultural impact on prevalence. However, low-to-middle-income nations may not have been able to afford the cost of screening methods or medical costs, thus distorting the prevalence rates from these areas.

Biological Etiology Considerations

Genetic Aspects

Despite a popular stress on finding one specific gene to implicate in ASD etiology, genetic involvement in ASDs appears to be heterogeneous, with no single genetic factor implicated as *the* causal variable in autistic neurodevelopment. Much research about the genetic etiology of ASDs has assumed that individual factors, such as a deleted gene, are associated with subclinical functional deficits, but that many factors (subclinical deficits) working in concert are sufficient to cause disorder (State, 2010, as cited in Tantam, 2012). Due to research in genetic and genomic projects, genetics seems to be the mysterious branch of ASD etiology. It is thus appropriate to examine ASD genetic etiology through three interrelated lenses: cytostructure mutations (changes to the chemical assembly and genetic makeup of chromosomes); heritability

(the proportion of differences between people due to genetics); and associated genetic disorders, in order to maximize public benefit from genetic research.

A chromosome is a cellular structure comprised of deoxyribonucleic acid (DNA), molecules that provide genetic information; ribonucleic acid (RNA), molecules that direct synthesis of new molecules; and proteins, chemical compounds that perform a variety of biological functions. Typical human cells contain 46 chromosomes that hold genetic information, which is passed to offspring during reproduction. Of the 46, two are sex chromosomes (an X chromosome from the mother, and either an X or Y from the father) that determine the sex of the offspring: Females have two X chromosomes, while males have one X and one Y.

A gene is a unit of heredity consisting of a segment of DNA or RNA in a chromosome that encodes instructions for the production of molecular structures important in the organism; the process of transferring genetic information from gene to gene product is called *gene expression*. DNA is wound into a double helix in chromosomes. In gene expression, RNA “unzips” the DNA double helix and creates a complementary duplicate of the information, and this information directs specific biological mechanisms. During this transcription process, mutations such as deletion, inversion, or duplication may occur, and these affect the accurate transfer of genetic information. Genetic encoding and expression are vital for the replication of almost all cellular structures in the human body, and for passing on traits to offspring.

Mutations of cytostructure. At a cytostructural level, chromosomal variations such as deletions, duplications, and inversions (collectively referred to as copy-number variations, or CNVs) create cellular DNA anomalies that account for some ASD cases (Tantam, 2012). CNVs may be inherited, or can occur *de novo*, meaning that they occur without inheritance.

Both deletions and duplications occur during misalignment of homologous chromosomes in cellular division, resulting in asymmetrical gene exchange (Tantam, 2012). A chromosome may not receive genes, which is deletion; a chromosome may also conversely receive extra genes, which is duplication. Inversions occur when the crossover process between homologous chromosomes results in a fractured chromatid on one or both chromosomes (Tantam, 2012). DNA polymerase, a restructuring catalyst enzyme, will reassemble the chromatid, but may do so with the genetic order reversed. CNVs can affect over 1000 bases in many chromosomal regions, altering millions of bases in the genome (Allen & Courchesne, 1998, as cited in Tantam, 2012). On such a large scale, CNVs can deactivate or overactivate genes, and this abnormal gene expression may contribute to atypical neurodevelopment.

CNVs have thus been increasingly implicated in predisposition to, and presence of, ASDs. Sanders et al. (2011) conducted a multicenter, genome-wide analysis of rare *de novo* CNVs among simplex probands and implicated five chromosomal loci of risk when they presented with large, rare *de novo* CNVs: 7q11.23; 1q21; 15q13.2-13.3; 16p13.2; and 16q23.3 (p. 878). However, two loci are of special note for the purpose of this thesis.

The first intriguing locus is 7q11.23. Sanders et al. (2011) found that duplications in 7q11.23 were significantly associated with ASD between probands and siblings; *deletions* at 7q11.23 cause Williams-Beuren syndrome, a neurodevelopmental disorder characterized by extroverted and highly sociable behavior. Duplications at 7q11.23, such as those found by Sanders and colleagues, may thus express social factors converse to Williams-Beuren, marked by impaired social interaction, lack of empathy, and introversion, all hallmark criteria of ASDs. More research needs to be conducted about 7q11.23 to ascertain its significance as a chemical mediator in social interaction.

The second locus of interest is 15q13.2-13.3, which occurs along a common gene segment of implication, 15q11-13. Maternally inherited duplications of 15q11-13 “are the most frequently reported chromosomal aberrations in autism spectrum disorders” (Depienne et al., 2009). Abnormalities along 15q11-13 are also related to changes in social behaviors, and in the expression of GABA, an inhibitory neurotransmitter. This genetic segment is discussed at greater length in the “familial inheritance” and “associated genetic syndromes” subsections, where it is described as the location of Angelman and Prader-Willi syndrome mutations. The genetic information along this segment can be damaged in the mother or father’s chromosome and still cause symptoms related to those of ASDs.

Heritability and parental age.

Familial inheritance. Data from twin studies (Bailey et al., 1995; Hallmayer, 2011) indicate that ASDs have a concordance rate of 70-90% in monozygotic (identical) twins, while dizygotic (fraternal) twins have a rate of 0-10% (as cited in Abrahams & Geschwind, 2008). This denotes a strong genetic foundation for ASDs, because if factors like childhood environment or vaccines were dominant in etiology, then both monozygotic and dizygotic twins may have more equivalent concordance rates due to similar upbringing. Jorde et al. (1991, as cited in Abrahams & Geschwind, 2008) found that in children with affected siblings, the relative risk of ASD diagnosis increases 25-fold or more over the population prevalence.

In a study of ASD-affected three-sibling groups, Cook et al. (1997) found that among one trio, two siblings presenting with an ASD inherited a duplication at gene locus 15q11-13 from their mother (whose duplication occurred *de novo* from her father), while the third, unaffected sibling did not. This particular family exhibited familial inheritance, in which maternal inheritance led to ASD trajectories but paternal inheritance patterns did not.

Parental age.

Maternal age. Much emphasis has been placed on maternal age in ASD research, ostensibly because of the link between ASD neurobiology and *in utero* neurodevelopment. The mother provides the pre-, peri-, and immediate postnatal environment for a child with an ASD, so conditions and factors related to childbearing are reasonable topics to examine.

Logically, positive relationships between maternal age and birth defects dictate that, past a threshold age, higher maternal age would increase a child's risk of ASDs or increase the severity of an ASD. However, results from germane studies have been inconclusive, with many studies finding relationships and others failing to do so. Steinhausen et al. (1984), Cryan et al. (1996), Bolton et al. (1997), Matsuishi et al. (1999), and Larsson et al. (2005) found no associations between autism and maternal age, while Gillberg (1980), Gillberg and Gillberg (1983), and Glasson et al. (2004) found associations between the two (as cited in Baxter et al., 2007). Maternal age may also sensitize ASDs at a level similar to how it sensitizes other neuropsychiatric conditions or birth defects, meaning that even though advanced maternal age does seem to increase ASD development risk, this increase may be no greater than the increased risk for conditions like Down's syndrome or schizophrenia. Complicating the conflicting literature on maternal age is the inability to generalize operational definitions for concepts such as severity, because ASDs incorporate many separate deficits, and assessment can be based on any combination of thousands of tests.

Paternal age. While maternal age is a logical condition to study, paternal age may appear inconsequential in comparison. However, Lundstrom et al. (2010) examined the effects of paternal age on autistic-like (social, communicative, and non-social stereotypy/repetitive behavior) traits in children from a United Kingdom and Swedish twin cohort, and found

significant associations for paternal age on all three traits in the Swedish cohort and on two traits in the United Kingdom cohort. The associations between age category and trait were U-shaped, indicating that paternal age less than 25 years as well as 50 years or older increased risk for autistic-like traits. These data do not directly contrast findings of maternal age effects.

Oftentimes, maternal age studies examined intelligence of children with ASDs, while this study investigated diagnostic traits of entire twin cohorts. However, it is important to note that in this study, paternal age does not form a positive linear association with ASD risk as maternal age studies seem to do, but it appears to affect ASD risk at both the low- and high-age ends.

Both parents. In a combined cohort-sibling analysis of Danish individuals with ASDs, Thorlund Parner et al. (2012) found that for mothers less than 35 years of age, offspring ASD risk increased as the father's age increased, and vice versa for fathers less than 35 years of age. However, data did not indicate that when both parents were of advanced age, ASD risk was higher than when only the mother or father was of advanced age.

Lampi et al. (2013) found that among a Finnish national cohort, parental and maternal age were related to specific spectrum disorders. The paternal age range of 35 to 49 years was associated with childhood AD development in offspring, while a maternal age of 35+ years was associated with Asperger's Disorder, and a maternal age of 40+ years or ≤ 19 years with other pervasive developmental disorders (PDD-NOS, Rett syndrome, or childhood disintegrative disorder). Thus, if both parents are older than 35 years, risk for childhood autism and Asperger's Disorder are increased, and if the father is 35+ years and the mother 40+ years, then the child has increased risk of childhood autism, Asperger's, and other pervasive developmental disorders. This study further defines ASD development risk by breaking down risk by specific disorder, which may yield even more important data about parental age.

Associated genetic syndromes. The identification and comprehension of associated syndromes is relevant to this thesis because the first step toward better societal integration of individuals with ASDs is to understand the causes of ASDs at a biological level. Genetic syndromes such as Angelman syndrome, Prader-Willi syndrome, and Fragile X syndrome may only account for a small number of cases of ASD, but they are nonetheless useful in identifying candidate genes or gene groups.

Angelman syndrome. Angelman (1965) described three children with similarly atypical symptomologies: mental retardation (MR); seizures; ataxia (lack of voluntary muscular control); absent speech; dysmorphic facial features (e.g. prominent chin); and easily provoked laughter. Before the syndrome bore his name, Angelman dubbed these individuals *puppet children*, while Bower and Jeavons (1967) modified this designation to *happy puppet syndrome* in further examinations of such individuals (as cited in Clayton-Smith & Pembrey, 1992). These names were derived from the ataxic symptoms, absent speech, and common wide smile of affected individuals. Angelman syndrome is relevant to ASD research because of their related symptomologies (communicative deficits, social interaction changes, and restricted movement) and implicated genetic regions.

Knoll, Nicholls, and Lalande (1989) and Nicholls et al. (1991) reported that more than 50% of Angelman syndrome cases expressed inheritance of maternal *de novo* deletions along 15q11-13, with that percentage rising toward 80% with molecular genetic analysis; corroborating this, Malzac et al. (1998) stated that maternally inherited deletions along 15q11-13 are responsible for 70% of cases (as cited in Clayton-Smith & Pembrey, 1992).

Angelman syndrome, in stark contrast with ASDs, has one specific gene commonly implicated in its expression: the ubiquitin-protein ligase E3A (UBE3A) gene located in the

chromosomal region of 15q11-13. UBE3A is an enzyme with intracellular protein degradation function, and a lack of maternal expression (via deletion) of UBE3A is sufficient to explain the clinical deficits of Angelman syndrome (Nicholls & Knepper, 2001). This is not to say that maternal deletions of UBE3A are the only cause of Angelman syndrome, but there exists sufficient support that the hallmark symptoms of Angelman syndrome can be explained by one inherited gene. If UBE3A deletions and deletions along 15q11-13 express clinical Angelman symptoms similar to those of ASDs, then 15q11-13 may represent a locus of ASD-relevant communicative and motoric function.

Prader-Willi syndrome. Prader-Willi syndrome is a disorder classically characterized by excessive eating and preoccupation with food, resulting obesity, a compact and low-tone body, and underdeveloped sex organs. In addition to the hallmark symptoms, individuals with Prader-Willi syndrome also demonstrate behaviors that overlap with ASD symptomatology. These include compulsions dealing with food, compulsions to arrange objects, repetitive behaviors (especially skin picking), and poor social understanding (Dykens, Lee, & Roof, 2011; Dimitropoulos & Schultz, 2007). It is a sister syndrome to Angelman syndrome, as it is caused by inherited paternal deletion in gene region 15q11-13 or duplication of the maternal chromosome. Approximately 70% of Prader-Willi cases are from paternal deletion, and about 25% of cases are from maternal duplication, with the remaining 5% due to other genetic malfunctions that cause the paternal genes to not be expressed (Dimitropoulos & Schultz, 2007).

Because Prader-Willi syndrome develops from mutations of the same gene segment as Angelman syndrome and they both share symptomatology with ASDs, more research is needed regarding 15q11-13's expression between maternal and paternal inheritance. Angelman syndrome seems to greatly affect communication and gross motor movement but Prader-Willi

syndrome involves repetitive and compulsive behaviors and social deficits, so 15q11-13 may be domain-specific based on which parent's chromosome is responsible for the individual's mutation.

Fragile X syndrome. Fragile X syndrome is a relatively common genetic disorder, affecting 1 in 3600 male births and 1 in 4000-6000 female births. The premutation (a change to the gene that does not create a new phenotype) is caused by an inactivation of the Fragile X mental retardation 1 (FMR1) gene at Xq27.3 (Tantam, 2012). The syndrome is named for the hallmark "fragile" appearance of the X chromosome under microscopy due to methylation (increase in hydrocarbon concentration) of a long gene segment. FMR1 codes for FMR protein, which is widespread in cellular activity; its absence decreases the concentration of superoxide dismutase 1 (SD1), a regulatory enzyme, which may in turn cause the development of ASD in Fragile X patients (Bechara et al., 2009, as cited in Tantam). Approximately 25% of males and 6% of females with Fragile X syndrome have an ASD, but only 1-2% of individuals with an ASD have Fragile X syndrome (Hatton et al., 2006, as cited in Abrahams & Geschwind, 2008). Differentially studying FMR protein and neuropsychology further between ASD-only individuals and Fragile X + ASD individuals may clarify how the regulatory effects of SD1 operate, and to what extent deficits of SD1 exist in the broad group of ASDs. For instance, if ASD-only children demonstrate similar mental retardation levels to Fragile X + ASD children but show more SD1, then the absence of SD1 in Fragile X + ASD may exacerbate cognitive symptoms and steer trajectories towards an ASD.

Neurology

Neurological abnormality among individuals with ASDs is widely documented. However, these findings are not always consistent, and contradictory results have been obtained

from many studies. Complicating the wide variability of ASDs is variable neuroanatomy between individuals, neurotypical or not. Even though one individual with an ASD may have a significantly lower amygdalar volume than controls, another individual with the same ASD and similar severity may have a normal amygdalar volume. In addition, departing from traditional post-maturation lesional studies, studies of ASDs often involve children, so neurodevelopment must be taken into account. This means that brain growth and individual system maturation must be considered in the search for neurological explanations of ASD development.

While single regions seem impossible to implicate in ASD development, it is clear that neurology is an important component of autism. Understanding the complex neurological underpinnings of ASDs is of vital importance in better grasping autism because differences in neurodevelopment interplay with psychological function to manifest various ASD trajectories. With the ultimate goal of better integrating individuals with ASDs into society, an investigation of neurological considerations is necessary.

Cerebellum. The cerebellum is a structure of the brain, located under the cerebrum, that fine-tunes accuracy and coordination in motor function. One major type of neuron in the cerebellum is the Purkinje cell; this type of cell is GABAergic, meaning that it works to produce GABA. A loss of Purkinje cells in the cerebellum has been reported widely in ASD cases (Kern, 2003; Palmen, van Engeland, Hof, & Schmitz, 2004; as cited in Schmitz & Rezaie, 2008). Fatemi, Reutiman, Folsom, and Thuras (2009) investigated GABA receptors postmortem in ASD and control brains, and found reduced levels in two GABA receptors in autistic cerebella. The gene for one of these receptors, GABA receptor subunit beta-3, is located along the 15q11-13 chromosomal interval, consistent with previous ASD implications (see the familial inheritance and associated genetic syndromes sections). Fatemi et al. (2010) also found decreased GABA

receptor subunit rho-1 protein and mRNA expression in postmortem autistic cerebella compared to neurotypical controls. Because of the cerebellum's role in fine-tuning movements and in coordination, which would require multiple sensory inputs, it is possible that less GABA (less inhibition) in the cerebellum would result in issues screening out sensory information or grouping it in useful ways, which is a symptom of ASDs.

Amygdala. The amygdala is a pair of almond-shaped brain structures located in the temporal lobes of the cerebrum. They are chiefly involved in memory consolidation and emotional regulation, and are thus often implicated in the social-emotional deficits of autism. Baron-Cohen et al. (2000) offered one such implication in the “amygdala theory of autism,” in which deficits of the amygdala cause the social and affective deficits that characterize ASDs. Individuals with ASDs and neurotypical controls were shown images of a pair of human eyes and asked to decide if they belonged to a male or female; eye stimuli were also paired with two opposite words (e.g. “sympathetic” and “unsympathetic”) and participants were asked to select the correct one. Functional MRI (fMRI, a common imaging technique that allows for the observation of brain regions active in a task) results indicated that autistic participants, as opposed to controls, did not activate their amygdala in the task of emotional recognition. Rather, autistic participants used other temporal lobe structures, possibly to compensate for amygdalar deficits.

Dalton et al. (2005) studied eye gaze fixation and neural activation upon presentation of emotional faces, familiar faces, and unfamiliar faces, and found that individuals with ASDs had significantly higher left amygdalar activation to emotional faces and significantly higher right amygdalar activation to familiar and unfamiliar faces than controls. While the emotional component seems to contradict Baron-Cohen et al.'s study, Dalton and colleagues used full-face

stimuli instead of only a pair of eyes. These activation patterns indicate that the amygdala does function in emotional processing, and functions in processing faces in all people in general. Amygdalar activation was also positively correlated with gaze fixation length, though autistic participants fixated their gaze significantly shorter lengths of time. Dalton and colleagues thus offer that longer eye gaze equates to more negative-emotional hyperarousal for individuals with ASDs, and that autistic participants fixating their gaze less is a maintenance behavior to avoid this negative arousal.

Amygdalar size in ASDs appears to have an abnormal developmental trajectory. The amygdala initially overgrows, but then returns to a volume comparable to that of a neurotypical individual. Sparks et al. (2002) found that in children aged 3 to 4 years, bilateral amygdalar volume was significantly larger than in age-matched controls, with the left amygdala 17.53% larger and the right amygdala 16.67% larger. Schumann et al. (2004) extended the research of Sparks et al; the study included both younger and older children, and found a 17% increase in both left and right amygdalar volume in young children with ASDs and no MR, corroborating Sparks et al.'s findings. The authors also found that in older children, there was no significant difference between ASD and control amygdalar volume, in line with current beliefs about amygdalar growth patterns. Denser growth patterns early in life may be due to decreased synaptic pruning, in which the number of neurons and connections are decreased. This decrease in pruning would make the neuronal connections in the brain less efficient, and may cause individuals with ASDs to use compensatory structures to make up for amygdalar deficits. This could be one cause of the social difficulties and emotional dysfunction in ASDs.

Corpus callosum. The corpus callosum (CC) is a flat layer of white matter under the cerebrum that provides neural connectivity between the left and right hemisphere of the brain. It

is the human brain's largest axonal pathway (Piven, Bailey, Ranson, & Arndt, 1997). Because of ASDs' functional impairments in several domains, CC abnormality is often targeted as a component of autism.

Using diffusion tensor imaging (a brain scan that allows water distribution, concentration, and direction in the brain to be scanned), Alexander et al. (2007) found that individuals with ASDs had lower CC volumes than neurotypical controls, both overall and within regions of the structure. Keary et al. (2009) also found significantly decreased total CC volume in ASD individuals, but found that some CC regions did not differ from controls. The low total volume yet unaffected regional volumes hint at the importance of studying individual CC regions' roles in ASD neurofunction. Alexander and colleagues (2007) also discerned two subgroups of the ASD sample based on fractional anisotropy (how restricted or packed fibers in the brain are) and mean diffusivity (a value for the average spread of water through the brain per area); one subgroup demonstrated low fractional anisotropy and high mean diffusivity, and the other demonstrated high fractional anisotropy and low mean diffusivity, which is similar to controls. The former had significantly lower CC volumes and lower performance IQ than the latter. Thus, information in the CC in ASD individuals may travel less efficiently between hemispheres, which affects sensory integration. Investigations of the CC must continue to examine the brain globally and regionally, and with as many volumetric and functional methods as possible to better ascertain the CC's role in ASD neurology.

Section Recap

Chromosome region 7q11.23 seems to be linked to social behavior, as deletions here can cause Williams-Beuren syndrome, a disorder characterized by extroverted and highly sociable behavior, and duplications are related to ASD development. Region 15q11-13 also appears to be

quite important because mutations can cause Angelman syndrome or Prader-Willi syndrome and alterations to GABA regulation; it is also the most commonly reported mutated region in ASD research. Paternal age may increase the risk of offspring developing ASDs at both the low and high ends, meaning that the father being too young or too old would increase ASD risk. Maternal age seems to increase ASD risk at the high end, but this risk increase may be the same as for any other developmental disorder. Alterations to ASD cerebella may cause a decrease in sensory filtering efficiency, which is compatible with ASD symptoms such as overresponsiveness or irritability. Amygdalar growth patterns are atypical in ASDs, with the amygdala initially overgrowing, but then reducing growth rate and meeting neurotypical amygdalar size. This overgrowth could reflect a deficit in synaptic pruning, which in turn would force individuals with ASDs to use compensatory neural structures. The amygdala is also implicated in the lack of eye gaze typical in autism, which affects social interaction and understanding. The CC seems to be reduced in size in ASDs. Its role in sensory integration and interhemispheric transfer points to atypical neuronal pathways and sensory integration, leading to deficits in information exchanges across hemispheres.

Neuropsychological Theories of ASDs

Neuropsychology refers to the clinical and scientific study of the relationship between brain systems and processes such as behavior, cognition, and speech. It can be conceptualized as a merged area of study that incorporates the biology and chemistry of neuroscience and the mental system analysis of cognitive psychology. This is useful for the purpose of this thesis because this section will draw on the biological concepts from the previous section, and will offer major neuropsychological theories that address ASD development or psychological

function. Juxtaposing these theories will also bring to light major differences between them, especially regarding which system or function is the most vital to ASD development.

Mind-blindness Theory

Mind-blindness Theory claims that children with ASDs are delayed in developing a theory of mind (ToM) and those delays leave children with ASDs with degrees of social impairment in inferring and predicting the thoughts, feelings, and beliefs of others (Baron-Cohen, 2009). The theory thus attempts to explain deficits in social reciprocity, interpersonal state understanding, and intrapersonal analysis of others' behaviors.

Theory of Mind. ToM is a mental capacity to identify and attribute mental states to oneself and others, to comprehend that others have mental states independent of one's own, and to evaluate others' behaviors based on those mental states (Tager-Flusberg, 2007). Although Premack and Woodruff (1978) developed the ToM hypothesis, Baron-Cohen, Leslie, and Frith (1985) were the first to attribute ToM deficits to ASDs.

Baron-Cohen et al. (1985) study. Baron-Cohen et al. (1985) employed a puppet-play paradigm of false belief known as the Sally-Anne test to investigate the ToM hypothesis (see Table 6 for experiment script and terms). If participants passed both controls but failed the Belief Question, that participant was classified as not employing a ToM. According to this hypothesis, they could thus infer that Sally would not know that Anne took her marble because Sally was not present to witness it, even though they themselves witnessed it. In other words, an individual with a ToM understands that Sally has a mental state separate from their own, and can analyze situations based on this.

Baron-Cohen et al. (1985) tested 20 autistic participants (mean age ≈ 11), 14 participants with Down's syndrome (mean age ≈ 10), and 27 normal controls (mean age ≈ 4.5) twice with the

Sally-Anne test. All participants passed the Naming Question, the Reality Question, and the Memory Question on both trials, and all participants but one (who had Down's syndrome) answered the Belief Question the same for both trials. Eighty-five percent of normal controls and 86% of Down's syndrome participants passed the Belief Question. In striking contrast, 80% of autistic participants *failed* the Belief Question, and all of these individuals pointed to the actual location of the marble in both trials (the box or the experimenter's pocket) (p. 42). Therefore, instead of simply pointing to the same spot both times, most autistic participants pointed to where the marble really was. Since these individuals knew where the marble was originally and where it was located when the questions were asked, which were confirmed by the reality and memory control questions, these results indicated to Baron-Cohen et al. that the participants who failed the Belief Question did not employ a ToM. These results were also taken in concert with other participant data, including verbal and non-verbal mental age. Autistic participants had higher verbal and nonverbal mental age than Down's syndrome participants, which Baron-Cohen et al. (1985) attributed to the Down's syndrome participants' more severe MR. Thus, according to the authors, the results of the Sally-Anne test do not reflect a product of intelligence level, but rather a system of cognitive empathy (inferring others' mental states).

Affected neural systems. Three brain regions have been identified as vital to mind-blindness theory: the anterior paracingulate sulcus, the temporo-parietal junction, and the amygdala. It is important to understand neural regions associated with neuropsychological theories because the cognitive and behavioral symptoms in ASDs arise from a biological basis.

Anterior paracingulate sulcus. According to Frith and Frith (1999), the most commonly observed activation present in neuroimaging during mentalizing tasks is a region in the middle-front of the brain called the anterior paracingulate sulcus. This region is a subregion of a

structure known as the anterior cingulate cortex, which is a C-shaped area of the prefrontal cortex (towards the rear of the frontal lobe). Interestingly, this region is also activated during tasks that involve monitoring one's own mental state. Frith and Frith offer that the anterior paracingulate sulcus is the neural region that self-monitoring of mental states emerges from, which would be a building block toward inferring others' states.

Temporo-parietal junction. Another region that often appears in neuroimaging during mentalizing tasks is the temporo-parietal junction, located just above the ears (Frith & Frith, 1999). Neurons in this region seem to form representations of "others": non-self agents who move of their own accord. Recognizing and understanding the behaviors and goals of others is crucial to ToM and mentalizing situations of empathy. For example, imagine that you are complicit in Anne's theft of the marble in the Sally-Anne test, and you are asked how to respond when Sally asks where her marble is without looking in her basket. You would need to know that Sally is not privy to the real location, that she will expect the marble to still be in her basket, that Anne's goal was to take the marble without Sally's knowledge, and that because your goal is to get off scot-free, you should say that the marble is still in Sally's basket in order not to implicate yourself and Anne. Though elaborate when written out, this type of situation can become intuitive to individuals with higher-order ToM, e.g. with neurotypical children by four years of age. However, this process of complex state attribution relies on cognitive empathy, goal attribution, and social understanding, which may each be partially disrupted in ASDs.

Amygdala. Frith and Frith (1999) also offer that the amygdala is frequently referenced as an important structure in ToM because of its role in eye gaze, which through joint attention may influence ToM. Ruffman, Garnham, and Rideout (2001) investigated eye gaze in autistic individuals and individuals with learning disabilities during the Sally-Anne test and found that

both groups answered the Belief Question equally well. However, individuals with moderate learning disabilities consistently looked at the correct location of the marble regardless of the answer they provided, while individuals with autism did not look at the correct location, even if the answer they provided was correct. This methodology provides a new spin on that of Baron-Cohen et al. (1985), because passing the Sally-Anne test is not the final index, but rather another social factor with which to examine ToM.

Criticism. Some researchers asserted that Baron-Cohen and colleagues' (1985) methodology did not seem to leave room for any gray area in ToM, since participants could only pass or fail. Tager-Flusberg (2007) offered that this system fostered the idea that "autism could be defined as the 'absence' of a theory of mind," and that it too quickly simplified a continuum of development into a "capacity indexed by passing or failing a single task" (p. 312).

One type of empathy involved in social function that is not accounted for in the ToM hypothesis directly is affective empathy, which is appropriately responding to inferences of others' mental states (Davis, 1994, as cited in Baron-Cohen, 2009). While it may seem logical to exclude affective empathy from the ToM hypothesis if no individuals with ASDs had a ToM (since an appropriate response is contingent on an appropriate inference), some individuals with ASDs in the study of Baron-Cohen et al. (1985) *did* pass the Sally-Anne test. This exclusion seems to limit the hypothesis' scope in addressing social dysfunction in ASDs, because it does not fully explain the full empathetic behavior of individuals with ASDs who employ a ToM but meet ASD subcriteria for social impairment. The amygdala's affective function may be an important component of developing social reciprocity, because it may aid in understanding goals and emotional states. Perhaps individuals with ASDs who pass the Sally-Anne test would

perform worse on hypothetical questions about how Sally feels about her missing marble or how Anne may feel if Sally is upset.

Empathizing-Systemizing Theory

Empathizing-Systemizing Theory (E-S) was developed by Baron-Cohen to rethink sex differences in cognition and to create both social and nonsocial factors for ASD investigation. This theory led to the Extreme Male Brain Theory (EMB, see below). E-S Theory posits that empathizing is a cognitive-emotional capacity to “predict and respond to the behavior of agents” (Baron-Cohen, Knickmeyer, & Belmonte, 2005); in essence, this means that empathizing is the ability to infer the mental states of others and appropriately respond to them. E-S Theory accounts for both cognitive and affective empathy (Baron-Cohen, 2009). The theory offers that systemizing is “the capacity to predict and to respond to the behavior of nonagentive deterministic systems by analyzing input-operation-output relations and inferring the rules that govern such systems” (Baron-Cohen et al., 2005). Simply, it is comprehending the processes of nonhuman systems. Baron-Cohen et al. state that at a population level, females are stronger empathizers and males are stronger systemizers. This is supported by 9% larger cerebrums in males, but a ratio of corpus callosum volume to total cerebral volume that is smaller in males. This suggests decreased interhemispheric connectivity and increased local connectivity in the male brain.

Strengths of E-S Theory. E-S Theory is more comprehensive than the mind-blindness theory, as E-S incorporates the social component of empathy and the nonsocial component of systemizing. A below-average empathetic capacity would explain the social and communicative deficits in ASDs, and a high systemizing capacity would explain narrow interests, repetitive behavior, and a need for constancy (Baron-Cohen, 2009). Additionally, according to E-S Theory,

high systemizing drive means that an individual will attempt to analyze all systems separately instead of generalizing similarities. This could explain why some individuals with ASDs have difficulty recognizing similar behavior topography steps in two different settings; for example, an autistic child may need to learn how to wash his hands with the sink at home, but also learn how to wash his hands with the sink at school. This child systemizes each process separately, and the differences between them become more salient than their many similarities (Baron-Cohen, 2009).

E-S Theory also has positive effects on the diagnosis and classification of ASDs. It may effectively differentiate ASDs from other disorders, because ASDs seem to have a distinct profile of low empathy and normal-to-high systemizing. It also eliminates the stigma of aberrance and poor function of ASD diagnosis, because rather than classifying ASDs into a separate category, E-S Theory focuses on comparing individuals with ASDs against individual differences in the neurotypical population, both between and within sexes. These comparisons are also not all negative; the typical profile is one of both below-average and above-average scores, and an individual's profile is thus on a continuum of population-wide behavior, rather than in a category solely for individuals with ASDs (Baron-Cohen, 2009).

Criticism. Little research has been conducted regarding affective empathy specifically, or about its interconnection with cognitive empathy. E-S Theory also may not apply as readily to individuals with lower-functioning ASDs as to individuals with high-functioning AD or Asperger's Disorder. Additional research is needed to investigate empathetic links, either through fMRI studies or through modifications to false belief or ToM tasks such as the Sally-Anne test, and to determine the generalizability of E-S Theory to all ASD diagnoses.

Extreme Male Brain Theory

An extension of E-S Theory, EMB Theory claims that ASDs represent impairments in empathizing and normal or above-average systemizing. After pairing these affected capacities with their relevant sexes, Baron-Cohen et al. (2005) inferred that ASDs reflect an expression of an “extreme” male neural system. Data from questionnaires about E-S allowed Baron-Cohen and colleagues to create “brain types” of Type B ($S \approx E$), Type S ($S > E$), Type E ($S < E$), Type Extreme S ($S \gg E$), and Type Extreme E ($S \ll E$) (see Table 5).

It would follow that if the male brain is geared more towards systemizing, and if ASDs are an expression of an EMB, then more males than females would develop ASDs. Examination of ASD prevalence sex ratios (per Fombonne, 2005 and CDC, 2012; see Epidemiology section) supports this deduction. Baron-Cohen et al. (2005) also provide percentages for sexes of participants per brain type, and found that none of the ASD individuals in the study were classified as Type Extreme E or Type E, while almost half (46.8%) were classified as Type Extreme S (see Table 1). These data match EMB Theory’s bases, in that individuals with ASDs were classified as having a male- or extreme male-type brain, and in that a much higher percentage of males than females were classified as such (no females were classified as Type Extreme S). It is also of note that in the general population, sex is a strong predictor of EMB brain type, but among individuals with ASDs, it is not (Goldenfeld, Baron-Cohen, & Wheelwright, 2005).

Baron-Cohen et al. (2005) account for these differences by citing hormonal imbalances in the ASD fetal brain. Testosterone, the chief male sex hormone, binds to androgen receptors and enter the brain and its cell nuclei. Testosterone influx decreases normal cell death, affects connectivity patterns and GABA regulation, and increases dendritic spine growth, meaning that

the neurons overgrow. The amygdala (see the neurology section above) is one region that Neural regions with high androgen receptor bonding include the cerebellum, amygdala, and corpus callosum (Baron-Cohen et al., 2005). If ASDs do indeed represent an extreme male brain, it is possible that this is a result of a hormonal imbalance in the ASD fetal brain.

In order to better understand the relationship between sex differences and ASDs within the EMB Theory, more research is needed focusing on female ASD experience. A larger study than Baron-Cohen et al.'s may discover females who are classified as Type Extreme S, and the data from these individuals may enrich the understanding of the empathizing and systemizing capacities as they relate to sex.

Sensory Processing Dysfunction

While ASDs affect many domains of bodily function that are outwardly perceivable to observers, one domain that is affected but not outwardly visible is sensory experience. Many individuals with ASDs are underresponsive and seek to generate their own sensory events to compensate, which is sometimes manifested as repetitive behaviors (Tomchek & Dunn, 2007). Tactile sensitivity is also reported, with oversensitivity to being touched or during grooming.

A portion of the literature about the ASD sensorium comes from self-report from writers with ASDs. One noteworthy autistic author and animal rights activist is Temple Grandin, who offered that she is “a totally visual thinker... [she doesn't] think in generalities” (Hoey, 2012). Because of this, she was able to draw cattle chutes in great detail to the point where she “could actually test run the equipment in [her] mind... [She] just thought everyone could do that” (Hoey, 2012). This phenomenon of being able to picture objects in great detail and evaluate their kinetic motion is not unique; another prominent historical individual who reported the same sensory style was Nikola Tesla (see below).

Tomchek and Dunn (2007) used the Short Sensory Profile to compare 281 children with ASDs against age-matched neurotypical controls and found that 95% of ASD subjects showed some level of sensory dysfunction on their Short Sensory Profile total score. The ASD group also demonstrated profiles that were significantly different than controls on 92% of all presented items, on all sections of the survey, and on the total score. The three sections of the survey with the greatest differences between control and ASD groups were underresponsiveness to stimuli/seeking sensation, auditory filtering (screening ambient noise and focusing on important noises), and tactile sensitivity (Tomchek & Dunn, 2007). Similarly, in a meta-analysis of 14 studies of sensory processing in ASD children, Ben-Sasson et al. (2009) found that the greatest difference between children with ASDs and controls was in underresponsiveness, and the third-greatest difference was in sensation seeking.

The profiles of both underresponsiveness and overresponsiveness may be related to neurological abnormalities in the CC and the cerebellum. If information is not passed efficiently through the CC between hemispheres, underresponding to stimuli may occur, because the proper amount of neural response is not transferred. This could explain why repetitive behaviors or stereotypy occur in ASDs, because these behaviors increase the amount of sensory stimulation occurring at a given moment. Conversely, overresponding to sensory information could occur if the cerebellum fails to properly blend the senses together and screen out useless sensory information. This could account for tantrums or irritability in ASDs, as well as a need for sameness and compulsive behaviors. If an individual with an ASD has a routine, both the body and mind are able to acclimate to that routine; changing the routine or the sensory experience of the moment could flood the ASD brain with too much information to function.

Section Recap

Mind-blindness Theory conjectures that individuals with ASDs lack a ToM, which disrupts their social judgment and understanding skills. Affected regions for this theory include the amygdala, the anterior paracingulate sulcus, and the temporo-parietal junction. While mind-blindness Theory does not take affective empathy into account, E-S Theory does. It is a less stigmatizing theory in that it established continua of empathizing and systemizing that any individual could be placed on instead of labeling groups who have or do not have a ToM. EMB Theory is an extension of E-S Theory, building on the concept of each individual having a certain empathizing and systemizing score. Individuals with ASDs, on a population level, seem to have much higher systemizing scores than empathizing scores, which classifies them as having an extreme male brain type. Baron-Cohen et al. (2005) thus speculated that ASDs reflect an extreme male brain organization. Sensory processing dysfunction is a possible consequence of CC and cerebellum deficits that could cause either overresponsiveness or underresponsiveness, and the visible expression of this in individuals with ASDs is repetitive movement or resistance to change.

Sociocultural Perspectives of ASDs

Historical Societal Views

Refrigerator mother theory. Until the late-middle 20th Century, ASDs were almost completely misunderstood or miscategorized as childhood mental illness. One prominent theory of ASD development in the 1950s and 1960s, the refrigerator mother theory, focused on the relationship between the individual with an ASD and their parents. The theory was based on the notion that parents who were emotionless with their young children caused those children to develop autism. Kanner (1949) wrote that autistic children were subject to “parental coldness,

obsessiveness, and a mechanical type of attention to material needs only.... They were left neatly in refrigerators which did not defrost. Their withdrawal seems to be an act of turning away from such a situation to seek comfort in solitude.” Bettelheim (1967) also proposed that parental detachment led to ASD development in a child. This theory has been completely debunked, but it represents a fundamental misunderstanding of ASDs as recently as 45 years ago. It also fits nicely in the context of the larger psychological theories of that time, with social development stressed as crucial for correct psychological growth.

Retroactive diagnosis of historical figures. Because ASDs are now rooted in the public conscious and because diagnoses have changed over time, many notable historical scientists and artists have been retroactively “diagnosed” by historians or researchers with an ASD, especially with Asperger’s. Some such figures include Wolfgang Amadeus Mozart, prodigious classical composer (Fitzgerald, 2005); Isaac Newton, prolific mathematician and physicist who developed calculus and laws of physics (James, 2003); Nikola Tesla, inventor and engineer who pioneered alternating current electrical power (Blume, 1997); and Albert Einstein, renowned theoretical physicist (James, 2003). James consulted Simon Baron-Cohen (see Amygdala, E-S theory, and EMB theory sections above) about the possibility of Newton and Einstein having had an ASD, and Baron-Cohen confirmed that based on current criteria and reports of Newton’s and Einstein’s peculiar behaviors, it is likely that they would have fallen on the autism spectrum. Both men reportedly had great difficulty forming social relationships early in life, which continued to some degree into adulthood.

Contemporary Perspectives

Theories and research about ASDs have largely been compatible with the prevailing psychological approach. For instance, since the Cognitive Revolution of the late 1950s, ASD

research has been less behaviorally focused and more cognitively focused. In addition to changes to research style, diagnostic strategies and goals changed. In the aftermath of these changes, ASD rates skyrocketed.

Increasing ASD rates. As autism became less of a categorical disorder and more continuum-based, two things happened. First, autism's entry in diagnostic manuals such as the DSM was restructured and placed alongside other disorders that were not previously separate, such as Asperger's Disorder or PDD-NOS. When atypical and less severe forms of ASDs were classified as separate disorders under the autism umbrella, the medical community was suddenly able to diagnose children who did not previously meet criteria for an autism diagnosis. This diagnostic shift could be thought of as the formal aspect of the diagnosis rate increases over the past 30 years. The informal aspect may be that the medical community began to stress ASD diagnosis once the criteria changed and societal awareness of diagnoses increased, because it stands to earn more revenue from individuals who need follow-ups, assessments, and medications. Taken together, the diagnostic and clinical changes in ASDs account for much of the historical increase in ASD rates but not necessarily all of it.

MMR vaccine. One attempt at the end of the 20th Century to find the cause of ASDs was with the measles, mumps, and rubella (MMR) vaccine. In 1998, Wakefield et al. published an article in the *Lancet* that linked the MMR vaccine to autism development. The authors claimed that parents of eight of the 12 autistic subjects reported that their children developed behavioral symptoms days after MMR vaccination. Wakefield et al. also stated that 11 of the 12 subjects had gastrointestinal disorders, and that these two symptomatology were related to a disorder that they dubbed "autistic enterocolitis" that somehow linked the MMR vaccine, autism, and gastrointestinal symptoms (Deer, 2010). Deer (2009) reported that the study, which was far from

conclusive, did have societal effects: inoculation rates dropped from 92% to 80%. Vaccination became a suspect of causing autism.

However, in 2001 and 2002, controversy about Wakefield et al.'s claims ramped up. Scientists were unable to reproduce the findings of the 1998 *Lancet* paper. In 2004, *The Lancet* partially retracted the paper, and in 2010, the paper was fully retracted. In the same year, the General Medical Council (GMC) of the United Kingdom found that Wakefield's tests for the study were invasive and performed on a powerless group, and that Wakefield did not have review board approval for the tests (Triggle, 2010). He also gathered blood samples for £5 at his son's birthday party. The GMC ruled that Wakefield acted "dishonestly and irresponsibly" in conducting the study, and was found guilty of more than 30 charges (Triggle, 2010). The result of the GMC's findings was that Wakefield was stricken from the register of physicians who can practice in the UK. After the controversy over Wakefield et al. (1998) and replications of the study conflicted with the original findings, confidence in the MMR vaccine has been restored.

Treatment styles. In order for children with ASDs to be more behaviorally or socially well-tempered, therapies or treatments are often used. Pharmacological interventions include serotonin reuptake inhibitors and dopamine agents, and non-pharmacological treatments include applied behavioral analysis (ABA) and music therapy.

Pharmacological interventions. Selective serotonin reuptake inhibitors such as fluoxetine (Prozac), sertraline (Zoloft), paroxetine (Paxil), and fluvoxamine (Luvox) have been found to be effective in calming repetitive behaviors and improving social symptoms of ASDs. Nonselective serotonin reuptake inhibitors such as clomipramine (Anafranil) have also been found to be similarly effective (McDougle et al., 2000; DeLong, Teague, & McSwain Kamran, 1998, as cited in Palermo & Curatolo, 2004). In addition, the anti-anxiety effects of these

antidepressants may assuage some of the generalized anxiety symptoms in ASDs. Haloperidol (Haldol), a dopamine receptor agonist, seems to sooth symptoms of social withdrawal, irritability, overactivity, mood dysregulation, and stereotypies in ASDs (Cohen et al., 1980, as cited in Palermo & Curatolo, 2004).

Non-pharmacological treatments. ABA is essentially the application of behaviorism concepts to improve or modify observable human behavior through learning. It is a common treatment method for directing and maintaining behaviors in ASDs. A hypothetical example of ABA-style treatment for communication deficits is a therapist asking a child with AD what the child's address is, and then reinforcing each answer with any part of the correct address until the child can successful answer with their full address. Myers and Johnson (2007) offered that children with ASDs who received early, intensive ABA treatment made large, sustained improvements in language, academic performance, IQ, and adaptive behavior. ABA is intended to allow individuals with ASDs to acquire capacities and skills for application in education and in life, and to shape learning in a more controlled style than in a general education classroom (Myers & Johnson, 2007). To this end, it is a viable intervention style for ASDs, because general education classrooms may provide too much stimulation for children with ASDs to focus and direct their attention. The direct observation inherent to ASD-specific ABA can also be valuable, because it allows a specialist to track a child's progress in separate domains (such as communication, socialization, or repetitive behaviors).

Music therapy is the use of music to stimulate, direct, or maintain behavior and to provide therapeutic treatment (American Music Therapy Association, 2013). An example of its application in ASDs is a therapist playing a song on the guitar and having a small group of ASD children do improvisational dance together, thus stimulating the children to not only coordinate

their own movements, but also socially interact with other children. Studies have found that individuals with an ASD prefer auditory stimuli to other types of stimuli if the auditory stimuli are music, and that these individuals will remain engaged with these music stimuli longer than their developmental-age-matched neurotypical controls (Blackstock, 1978; Kolko, Anderson, & Campbell, 1980; Thaut, 1987, as cited in Simpson & Keen, 2011). Music therapy may also foster affective development through the connection between music and emotion.

Common societal stereotypes

Hollywood films featuring autistic characters may serve as bellwethers for the social stereotypes of ASDs, as they are both reflecting and projecting society's opinions about autism through dialogue and plot. Common depictions of autistic characters center on savant syndrome, a condition in which performance in a limited number of specified areas, such as mathematic functions, musical instrumentation, or recall, is dramatically boosted (Treffert, 2009). Savant syndrome is relatively sensational, so stories of individuals with ASDs and savant syndrome are identified more in society (see Thomas Fuller and Kim Peek below, compared to similar individuals with no savant skills). The accepted incidence of savant syndrome is about 10% in autism, but perhaps only half of savants have autism; the other half have MR, central nervous system damage, or other developmental disorders (Treffert, 2009).

Savant syndrome has been reported for hundreds of years. Rush (1789, as cited in Treffert, 2009) documented the arithmetical skills of a slave named Thomas Fuller, who had limited cognitive abilities but could calculate large values with ease. When asked how many seconds a man who is 70 years, 17 days and twelve hours old had lived, he thought for 90 seconds, and then answered 2,210,500,800. A man working it out on paper told him that he was incorrect, but Fuller told him to account for leap years, which made the control match Fuller's

number (Treffert, 2009). Another notable savant was Kim Peek, who had amazing memory abilities in geography, music, history, sports, and other domains. He memorized over 6000 books, knew all of the US area codes and major city zip codes, and could read books by scanning one page with his left eye and the other page with his right eye (Treffert, 2009). MRI showed that Peek lacked a corpus callosum and also had other central nervous system damage. No corpus callosum meant that Peek's brain might have developed different connections for sensory integration and memory due to neuroplasticity, a natural change in neuron paths due to changes in the brain or environment.

Peek was an inspiration for Dustin Hoffman's character Raymond Babbitt in *Rain Man*; Babbitt is an autistic savant with amazing recall and mathematic computation abilities. He avoids eye contact and intense physical contact, and repeats Abbott and Costello's "Who's on first?". Though he is able to answer extremely difficult mathematical questions quickly and easily, he is unable to conceptualize money in the same mathematical frame. His value as a character (and thus as a human) is initially realized only because his abilities would allow his brother to win big at a casino; only as the movie closes does his brother accept him. Babbitt, to the audience, may appear to be a pathetic character. He also functions as a sort of human computer who does not express emotion but is able to surpass normal function. Another popular representation of savant syndrome in autism is the film *Mercury Rising*. The film revolves around Simon, an autistic nine-year-old with mathematical savant abilities who cracks a government security code that was thought to be unbreakable by any computer. Again, Hollywood portrays an autistic character as valuable only for their savant skills, and as a human computer who shows little emotion.

Not all films portray autism comorbid with savant behavior. Asperger's Disorder without savant syndrome is a prominent component of the film *Mary and Max*, an Australian claymation film. Max is an American with Asperger's Disorder, but he is not diagnosed until he is in his forties. His diagnosis allows him to see life differently and to make sense of his social awkwardness. Mary is a young Australian girl who randomly chooses Max as her overseas pen pal; his story inspires her to later become a psychologist, and she writes a book about Asperger's as a clinical disorder to be cured. Max is furious because he sees Asperger's as a vital part of himself, not as a disorder to cure. Max has no amazing computational skills, and despite difficulties, he is able to have friendships, to communicate, and to function daily.

Using films to gauge the societal stereotypes of autism provides some salient details. First, savant syndrome is commonly portrayed as a distinguishing characteristic of ASDs. Savant syndrome is sensational, and its presentation can be stretched to make a film's plot even wilder. Its presentation in the films, generally as a moment of witnessing the character do a complex computation, is intended almost as a subconscious narrative saying, "Wow, this character really is autistic". Without savant syndrome, the character may be aloof and difficult to the audience, but not necessarily autistic. Second, the autistic character often swings from mysterious to superhuman when their savant skills are presented to the audience, and in either case, it is the differences and not the similarities between individuals with ASDs and neurotypical people that are stressed. Third, definitions of ASDs differ between films and sometimes are not used in films at all; this leaves the audience with loose ends in terms of what exactly constitutes ASDs. ASDs may thus seem more mysterious, contributing to social confusion about how the spectrum works and why a spectrum is needed.

Combating Autism Act of 2006

Signed into law by President George W. Bush, the Combating Autism Act of 2006 is a piece of legislature created to fund ASD research and to disseminate useful ASD information through government agencies. Funds are allocated to the CDC to create epidemiological surveillance programs; to the National Institutes of Health to research ASDs; and to the Interagency Autism Coordinating Committee of the Department of Health and Human Services, which organizes and directs research across agencies (“S.843”, 2006). From 2006 to 2011, the Combating Autism Act authorized nearly \$945 million of ASD-related funds; in 2011, President Obama renewed the act until 2014, authorizing another \$693 million to fund further research and services (“President Obama”, 2011). This renewal represents an increase in funding per year (\$189 million/year to \$231 million/year) and raises the total Act authorization to over \$1.6 billion. While the bill doubtless contributes generously to ASD research through financial support to government bureaus, greater financial efficiency might occur if a more centralized ASD bureau replaced the Interagency Autism Coordinating Committee of DHHS and overtook the research projects of the CDC and National Institutes of Health. This would remove the need for interagency organization and its funding, and synergize ASD research projects. Because of how important ASD research is, it is crucial that the maximum amount of funding is available.

Autism Rights Movement

The Combating Autism Act could be seen as an example of a governmental response to the societal perception of ASDs as a widening epidemic that must be cured. In opposition to this emphasis, groups such as the Autism Acceptance Project are working toward a societal acceptance of autism as another way of viewing the world, rather than as a set of negative symptoms that should be eradicated to better resemble neurotypical behavior. Most groups do

not oppose treatments for ASDs, but instead want to focus on the positive aspects of ASDs while alleviating negative ones to improve quality of life. Aspies for Freedom, a group led by Gareth Nelson in the UK, even seeks to have individuals with ASDs recognized as minorities instead of people with disabilities (Saner, 2007).

With more funds and attention directed at autism causes and genetic markers for ASDs, a common fear among autism rights groups is that definitive prenatal tests will soon be available during pregnancy. With extremely high rates of fetal abortion after prenatal diagnosis of disorders like Down syndrome (92% in the UK and Europe, see Mansfield, Hopfer, & Marteau, 1999), it is not inconceivable that abortion rates would be high for fetuses with ASDs, especially in the case of low function if prenatal diagnoses can be accurate regarding severity. This is especially poignant given that society may have a more positive opinion of Asperger's Disorder than of AD (or an idea of what PDD-NOS is). Assuming Down syndrome rates were matched, extinguishing 90 to 95% of AD cases and a substantial, but probably lower, amount of Asperger's Disorder cases would surely reshape both clinical and research emphases of ASDs.

Section Recap

Scientific research of ASDs sharply increased in the late 20th Century, just before society caught wind of ASDs as an epidemic that was getting worse. Unfortunately, the societal response lagged in understanding ASDs compared to scientific investigations. At times, naïve or unethical science made this schism worse (see “refrigerator mother theory” and “MMR vaccine”). Historical figures being retroactively diagnosed with ASDs may also be an extension of a misunderstanding of autism at a societal level, because in cases where ASDs are unlikely, quirkiness or giftedness is equated with dysfunction or disorder. Changes to diagnostic style (categories to continua) and clinical strategies (new ASDs to diagnose) accounts for most of the

sharp increase in autism rates since the 1980s, but not all; some environmental factors such as the MMR vaccine have been ruled out, but not all possible explanations have been explored. Pharmacological treatments such as Zoloft, Prozac, Anafranil, and Haldol are effective in calming anxiety or behavioral symptoms of ASDs, while non-pharmacological treatments like ABA and music therapy are useful in the development and maintenance of life skills. It is important to take into account that ASDs do not always represent a severe disorder to overcome for all individuals who have it. Instead, greater acceptance of ASDs as another way of experiencing the world rather than as a handicap would permit more integration of individuals with ASDs into society.

Conclusion

When biological, neuropsychological, and sociocultural aspects of ASDs are taken in concert, it is plain to see that autism is an incredibly heterogeneous and complicated disorder. Therefore, using only one perspective in an examination of ASDs may leave gaps in understanding its complexity. The biological perspective is essential because it accounts for the basic physiological differences and deficits in ASDs. This information is of vital importance to the comprehension of the neuropsychological perspective of ASDs, in which biological differences are linked to psychological and behavioral functions. Finally, an understanding of the biological and neuropsychological perspectives allows a more complete understanding of the sociocultural awareness and beliefs about ASDs. Combining these three perspectives creates a more well-rounded understanding of ASDs in society, and this understanding is necessary for the appropriate integration of individuals with ASDs.

The search for a clear-cut cause of ASD development has fallen flat, but some major components of ASD biology have been identified through research. These include:

chromosomal segment 15q11-13, notable for its role in Angelman and Prader-Willi syndromes and in CNVs; Purkinje cell loss in the cerebellum; abnormal amygdalar growth patterns; and low CC volume. Neuropsychological theories of ASDs include the EMB theory, E-S theory, mind-blindness, and sensory processing dysfunction. Socioculturally, autism is often viewed as an epidemic, but there exists a movement to shift opinions of ASDs from disability to difference in experience while ameliorating dysfunctional or injurious symptoms.

The next step toward better integration of individuals with ASDs into society is a clinical emphasis on treating symptoms of ASDs that lead to self-harm or affect daily function, and a cultural emphasis on not attempting to “correct” or “cure” non-injurious or dysfunctional ASD symptoms to make them seem more neurotypical. ASDs may be classified as neurodevelopmental disorders, but perhaps society would benefit from seeing them more as neurodevelopmental re-orders.

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Table 1

DSM-IV-TR Diagnostic Criteria for 299.00 Autistic Disorder

<p>(I) A total of six (or more) items from (A), (B), and (C), with at least two from (A), and one each from (B) and (C)</p> <p>(A) qualitative impairment in social interaction, as manifested by at least two of the following:</p> <ol style="list-style-type: none">1. marked impairments in the use of multiple nonverbal behaviors such as eye-to-eye gaze, facial expression, body posture, and gestures to regulate social interaction2. failure to develop peer relationships appropriate to developmental level3. a lack of spontaneous seeking to share enjoyment, interests, or achievements with other people, (e.g., by a lack of showing, bringing, or pointing out objects of interest to other people)4. lack of social or emotional reciprocity (note: in the description, it gives the following as examples: not actively participating in simple social play or games, preferring solitary activities, or involving others in activities only as tools or "mechanical" aids) <p>(B) qualitative impairments in communication as manifested by at least one of the following:</p> <ol style="list-style-type: none">1. delay in, or total lack of, the development of spoken language (not accompanied by an attempt to compensate through alternative modes of communication such as gesture or mime)2. in individuals with adequate speech, marked impairment in the ability to initiate or sustain a conversation with others3. stereotyped and repetitive use of language or idiosyncratic language4. lack of varied, spontaneous make-believe play or social imitative play appropriate to developmental level <p>(C) restricted repetitive and stereotyped patterns of behavior, interests and activities, as manifested by at least two of the following:</p> <ol style="list-style-type: none">1. encompassing preoccupation with one or more stereotyped and restricted patterns of interest that is abnormal either in intensity or focus2. apparently inflexible adherence to specific, nonfunctional routines or rituals3. stereotyped and repetitive motor mannerisms (e.g hand or finger flapping or twisting, or complex whole-body movements)4. persistent preoccupation with parts of objects <p>(II) Delays or abnormal functioning in at least one of the following areas, with onset prior to age 3 years:</p> <p>(A) social interaction</p> <p>(B) language as used in social communication</p> <p>(C) symbolic or imaginative play</p> <p>(III) The disturbance is not better accounted for by Rett's Disorder or Childhood Disintegrative Disorder</p>
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Note. From *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition – Text Revision.*

Table 2

Restricted Behavior Scale – Revised Behavior Types and Examples

<p>Stereotypy: the repetition of movements that are socially purposeless, but provide sensory relief for the individual performing it.</p> <p><i>Examples:</i> hand flapping, in which a child moves his hands quickly as though he is trying to get something off of them; rocking back and forth; running objects across peripheral vision.^a</p> <p>Self-injurious behavior: behavior with potential to cause harm (redness, bleeding, etc.) to the performer; behaviors can be both stereotypic and self-injurious.</p> <p><i>Examples:</i> picking at the skin; hitting one’s head against the floor or wall; biting oneself.</p> <p>Compulsive behavior: behavior intended to follow rules (internal or external) or patterns.</p> <p><i>Examples:</i> arranging toy cars in a line by size; stacking blocks by color.</p> <p>Need for sameness: insistence upon not changing situations.</p> <p><i>Examples:</i> distress when plans change suddenly; becoming upset if toys are moved.</p> <p>Ritualistic behavior: insistence upon daily routines.</p> <p><i>Examples:</i> wearing certain clothes for each day of the week; dressing in a certain routine; eating the same foods every day.</p> <p>Restricted interests: narrowed focus, attention, or occupation on a few stimuli.</p> <p><i>Examples:</i> only playing with one toy car; talking often about one topic, like bugs or dinosaurs; only watching one television show.</p>
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Note. Definitions and examples of restricted behaviors of the Restricted Behavior Scale – Revised in AD. Adapted from Lam & Aman, 2007.

^aExamples from Schreibman, Heyser, & Stahmer, 1999, as cited in Cunningham & Schreibman, 2009.

Table 3

DSM-IV-TR Diagnostic Criteria for 299.80 Asperger’s Disorder

<p>(I) Qualitative impairment in social interaction, as manifested by at least two of the following:</p> <p>(A) marked impairments in the use of multiple nonverbal behaviors such as eye-to-eye gaze, facial expression, body posture, and gestures to regulate social interaction</p> <p>(B) failure to develop peer relationships appropriate to developmental level</p> <p>(C) a lack of spontaneous seeking to share enjoyment, interest or achievements with other people, (e.g., by a lack of showing, bringing, or pointing out objects of interest to other people)</p> <p>(D) lack of social or emotional reciprocity</p> <p>(II) Restricted repetitive & stereotyped patterns of behavior, interests and activities, as manifested by at least one of the following:</p> <p>(A) encompassing preoccupation with one or more stereotyped and restricted patterns of interest that is abnormal either in intensity or focus</p> <p>(B) apparently inflexible adherence to specific, nonfunctional routines or rituals</p> <p>(C) stereotyped and repetitive motor mannerisms (e.g. hand or finger flapping or twisting, or complex whole-body movements)</p> <p>(D) persistent preoccupation with parts of objects</p> <p>(III) The disturbance causes clinically significant impairments in social, occupational, or other important areas of functioning.</p> <p>(IV) There is no clinically significant general delay in language (e.g. single words used by age 2 years, communicative phrases used by age 3 years)</p> <p>(V) There is no clinically significant delay in cognitive development or in the development of age-appropriate self help skills, adaptive behavior (other than in social interaction) and curiosity about the environment in childhood.</p> <p>(VI) Criteria are not met for another specific Pervasive Developmental Disorder or Schizophrenia.</p>
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Note. From *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition – Text Revision*.

Table 4

DSM-IV-TR Diagnostic Criteria for 299.80 PDD-NOS

This category should be used when there is a severe and pervasive impairment in the development of reciprocal social interaction or verbal and nonverbal communication skills, or when stereotyped behavior, interests, and activities are present, but the criteria are not met for a specific Pervasive Developmental Disorder, Schizophrenia, Schizotypal Personality Disorder, or Avoidant Personality Disorder. For example, this category includes atypical autism --- presentations that do not meet the criteria for Autistic Disorder because of late age of onset, atypical symptomatology, or subthreshold symptomatology, or all of these.

Note. From Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition – Text Revision.

Table 5

E-S Theory brain types, percentiles, percentages, and classifications.

Brain Type	Extreme E	E	B	S	Extreme S
Brain Sex	Extreme female	Female	Balanced	Male	Extreme male
Defining Characteristic ^a	$S \ll E$	$S < E$	$S \approx E$	$S > E$	$S \gg E$
Percentile (per)	$\text{per} < 2.5$	$2.5 \leq \text{per} < 35$	$35 \leq \text{per} < 65$	$65 \leq \text{per} < 97.5$	$\text{per} \geq 97.5$
Female %	4.3	44.2	35.0	16.5	
Male %		16.7	23.7	53.5	6.1
AS ^b /HFA ^c %			12.8	40.4	46.8

Note. Adapted from Baron-Cohen, Knickmeyer, & Belmonte, 2005.

^aDifferences between Systemizing (S) and Empathizing (E) scores based on empathy and systemizing quotients from questionnaires from Baron-Cohen et al., 2005.

^bAS = Asperger syndrome, presented in text as Asperger’s Disorder.

^cHFA = High Functioning Autism.

Table 6

Experiment Script for Baron-Cohen et al. 's (1985) Sally-Anne test

<p>1. Participant is seated across a small table from the experimenter. In front of the participant to the left are a basket and a doll. In front of the participant to the right are a box and a doll.</p> <p>2. The experimenter introduces the dolls to the participant. The doll to the left is named Sally; the doll to the right is named Anne.</p> <p>3. The experimenter asks the participant to name the two dolls (the Naming Question).</p> <p>4. Sally places a marble in the basket in front of her.</p> <p>5. Sally leaves the scene.</p> <p>6. Anne takes the marble out of Sally's basket and hides it in her box.</p> <p>7. Sally reenters the scene.</p> <p>8. For trial 1, proceed to step 9. For trial 2, the experimenter places the marble in their pocket.</p> <p>9. The experimenter asks, "Where will Sally look for her marble?" (the Belief Question).</p> <p>10. The participant points to a location in the scene.</p> <p>11. The experimenter asks, "Where is the marble really?" (the Reality Question).</p> <p>12. The experimenter asks, "Where was the marble in the beginning?" (the Memory Question).</p> <p>13. If the participant correctly answered the Reality Question and the Memory Question, and if the participant pointed to the basket during the Belief Question, then they have employed a theory of mind. If the participant answers the Memory and Reality Question correctly and points to the current location of the marble (the box for trial 1, the pocket for trial 2), or if they answer either control incorrectly, then they have not employed a theory of mind because they did not take the doll's beliefs into account.</p>
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